Background. The quadrivalent live attenuated influenza vaccine (LAIV4) showed reduced effectiveness for the A/H1N1 component of the vaccine in 2013–2014 and 2015–2016. To address this, new assays were used to identify H1N1 LAIV strains with improved replicative fitness and immunogenicity. In this study, we compared the shedding and immunogenicity of a new A/H1N1 strain (A/Slovenia), selected using the new assays, to a previous strain (A/Bolivia) with reduced effectiveness.

Methods. Two hundred children aged 24 to <48 months were randomized 1:1:1 to receive two doses of a quadrivalent formulation of 2015–16 LAIV or a trivalent formulation of 2015–2016 LAIV, both containing the H1N1 A/Bolivia strain, or a quadrivalent formulation of the 2017–2018 LAIV containing the new H1N1 A/Slovenia strain (NCT03143101). Nasal and serum immune responses were assessed before Doses 1 and 2, and 28 days after Dose 2. Nasal shedding was assessed on Days 2, 3, 4, 5, and 7 after Dose 1, and Days 2, 4, and 6 after Dose 2. Solicited symptoms, adverse events, and serious adverse events were collected. Statistical testing was limited to the prespecified primary endpoint of hemagglutination inhibition (HAI) antibody responses.

Results. A higher proportion of children shed the A/Slovenia vaccine strain than the A/Bolivia strain on Days 4–7 after Dose 1. The study met its primary endpoint, with significantly higher HAI antibody responses for the A/Slovenia strain after both the first and second doses of vaccine (Figure 1). Neutralizing antibodies and nasal immunoglobulin A (IgA) antibody responses were higher for the A/Slovenia than the A/Bolivia strain for both the trivalent and quadrivalent vaccine formulations. HAI antibody seroconversion rates (≥4-fold increase from baseline) for the A/Slovenia strain were similar to those seen in previous studies in which the H1N1 vaccine strain was highly efficacious (Figure 2). There were no significant safety findings.

Conclusion. The new H1N1 A/Slovenia strain demonstrated improved immunogenicity compared with a previous strain with reduced effectiveness, and immune responses comparable to a highly efficacious H1N1 LAIV strain. These results support the use of LAIV4 as an important vaccine option.

Figure 1.

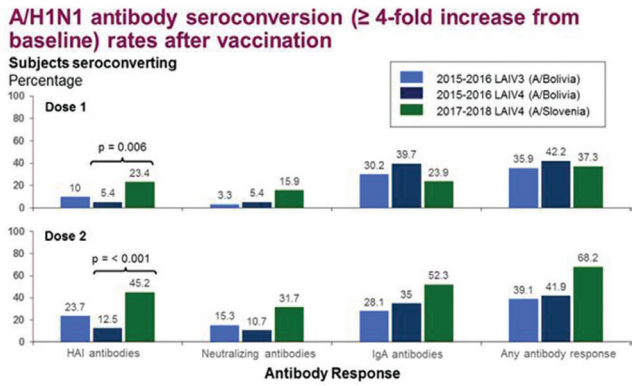
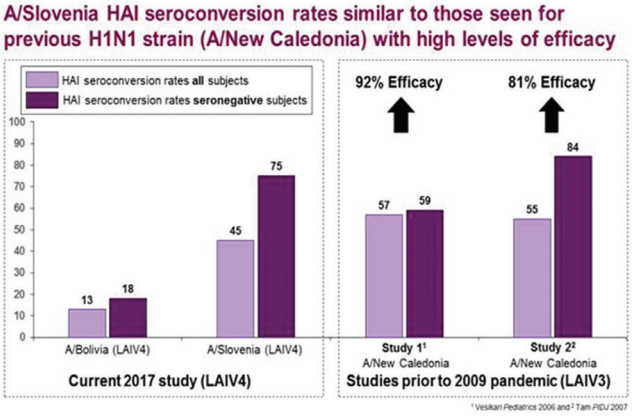


Figure 2.



Disclosures. **R. Mallory**, MedImmune: Employee, Salary. **A.C. Nyborg**, MedImmune: Employee, Salary. **R. Kalyani**, MedImmune: Employee, Salary. **L.F. Tsai**, MedImmune: Employee, Salary. **S.L. Block**, AstraZeneca: Investigator, Research grant. **F. Dubovsky**, MedImmune: Employee, Salary.

1955. A Randomized, Double-Blind Study to Evaluate the Safety, Tolerability, and Efficacy of Caspofungin vs. Amphotericin B Deoxycholate in the Treatment of Invasive Candidiasis in Neonates and Infants ≤3 Months of Age

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Background. *Candida* species are the most common fungal pathogens in infants aged <1 year. Current antifungal regimens such as amphotericin B deoxycholate (dAmB) are associated with serious toxicity and multiple drug-drug interactions. The echinocandin caspofungin has less toxicity than dAmB and is approved for candidemia and other invasive *Candida* infections (ICI) in pediatric populations aged ≥3 months to 17 years. We investigated the efficacy of caspofungin in patients aged ≤3 months in ICI.

Methods. This phase 2, multicenter, randomized, double-blind, comparator-controlled study (Protocol MK0991-064; NCT01945281) enrolled patients aged ≤3 months with culture-confirmed ICI ≤96 hours before study entry. Patients were randomized 2:1 to IV caspofungin 2 mg/kg once daily or IV dAmB 1 mg/kg once daily. Primary endpoint was fungal-free survival (FFS) at 2 weeks post-therapy. Initial target sample size was 90 patients.

Results. Fifty-one patients were enrolled. The study was terminated early due to low enrollment after >3.5 years' recruitment. Median age (min–max) at enrollment = 22 days (7–88 days); male = 53.2%; median birth weight (min–max) = 1445 g (510–4,175 g); median baseline weight (min–max) = 1,860 g (425–6,540 g); median gestational age (min–max) = 30.4 weeks (26–41 weeks). *C. albicans* was the most common species isolated. Forty-nine patients received treatment (caspofungin, $N = 33$; dAmB, $N = 16$); two additional patients did not have confirmed infections at study entry. Overall, 47 patients were included in the full analysis set population (caspofungin, $N = 31$; dAmB, $N = 16$). FFS at 2 weeks post-therapy was 71.0% (22/31) in the caspofungin arm and 68.8% (11/16) in the dAmB arm (difference, –0.9% [95% CI, –24.3%, 27.7%]). 84.8% (28/33) of patients in the caspofungin arm and 100% (16/16) in the dAmB arm had ≥1 adverse event (AE); anemia (10/33 and 8/16, respectively) and sepsis (3/33 and 5/16, respectively) were the most common. Two patients in each arm had investigator-assessed treatment-related AEs. Serious AEs (SAEs) were 21.2% (7/33) in the caspofungin arm and 56.3% (9/16) in the dAmB arm; 5 patients died, 2 (6%) in caspofungin arm, and 3 (19%) in dAmB arm. All SAEs and deaths were unrelated to study drug.

Conclusion. Among neonates and infants with confirmed ICI, FFS at 2 weeks was similar in the caspofungin and dAmB treatment arms. Patients who received caspofungin experienced fewer AEs and SAEs.

Disclosures. **J. Kim**, Merck & Co., Inc.: Employee, Salary. **F. Lambey Nakwa**, Merck & Co., Inc.: Principal Investigator, Research support. **F. De Araujo Motta**, Merck & Co., Inc.: Grant Investigator, Grant recipient. **P. Salcedo Lozada**, Merck & Co., Inc.: Investigator, Research support. **D. Alabaz**, Merck & Co., Inc.: Investigator, Research support. **H. Liu**, Merck & Co., Inc.: Employee, Salary. **K. Bloise**, Merck & Co., Inc.: Employee, Salary. **M. B. Dorr**, Merck & Co., Inc.: Employee and Shareholder, Salary. **L. J. Anderson Gaffney**, Merck & Co., Inc.: Employee, Salary. **N. Kartsonis**, Merck & Co., Inc.: Employee and Shareholder, Salary.

1956. Persistence of Immune Response and Safety of an Adjuvanted Recombinant Zoster Vaccine in Older Adults Previously Vaccinated with a Live-Attenuated Herpes Zoster Vaccine: End-of-Study Results of a Phase III, Group-Matched, Clinical Trial

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Background. Herpes zoster (HZ), caused by reactivation of varicella-zoster virus (VZV), typically manifests as a dermatomal rash and can result in complications, such as postherpetic neuralgia. HZ risk increases with age due to age-related decline of immunity. At time of study start, Zoster Vaccine Live (ZVL), containing live-attenuated VZV was recommended for vaccination in adults ≥60 years of age. Efficacy of ZVL declines with time since vaccination and increasing age. We evaluated immunogenicity and safety of Adjuvanted Recombinant Zoster Vaccine (RZV) containing truncated form of VZV glycoprotein E (gE) in adults vaccinated with ZVL ≥5 years before (HZ-PreVac) and ZVL-naïve adults (HZ-NonVac). In October 2017, the Advisory Committee on Immunization Practices recommended revaccination of ZVL recipients with RZV, based on available data, including 1 month (M) post-dose 2 results of this study (M3). Here we present immunogenicity and safety results up to 12 months post-dose 2 (M14).

Methods. In this phase III, multi-center study (NCT02581410), open-label, 2 parallel groups of group-matched adults ≥65 years of age, HZ-PreVac and HZ-NonVac, received 2 RZV doses 2 months apart. Humoral and cellular immune responses were evaluated at various time points up to M14. Solicited and unsolicited adverse events

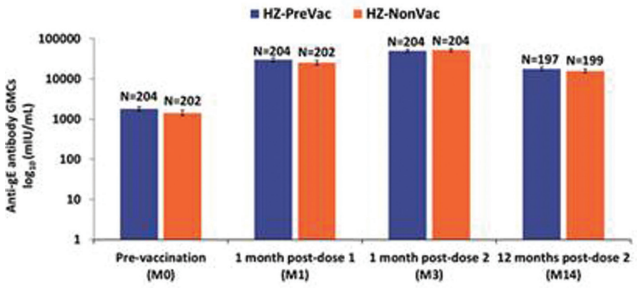
(AEs) were recorded for 7 and 30 days post each dose, respectively. Serious AEs (SAEs), HZ cases and potential immune-mediated diseases (pIMDs) were recorded throughout the study.

Results. 215 participants were vaccinated in each group. No apparent differences, in pre-vaccination and persistence values of the anti-gE antibody GMCs (Figure 1) and CD4[2+] T-cell frequencies (Figure 2) were observed between HZ-PreVac and HZ-NonVac, up to M14. No clinically relevant differences in frequencies of solicited AEs, unsolicited AEs or SAEs between the two groups were observed. Six pIMDs (two in HZ-PreVac group and four in HZ-NonVac group), were reported up to M14 (Table 1).

Conclusion. In both groups, RZV-induced humoral and cellular immune responses persisted above baseline up to M14 at similar levels, irrespective of previous ZVL administration. Safety profile was similar regardless of previous ZVL vaccination.

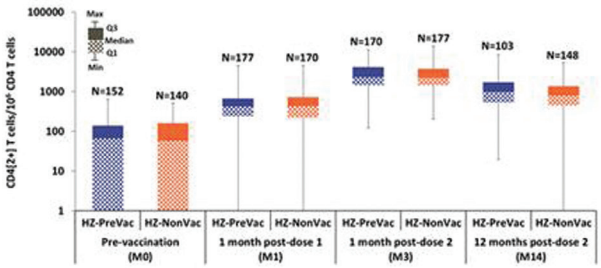
Funding: GlaxoSmithKline Biologicals SA.

Figure 1. Anti-gE antibody geometric means concentrations (adapted ATP cohort for immunogenicity) prior to and following RZV vaccination



gE, glycoprotein E; **ATP**, according-to-protocol; **GMCs**, geometric mean concentrations; **HZ-PreVac**, participants ≥65 YOA vaccinated with zoster vaccine live (ZVL) ≥5 years earlier; **HZ-NonVac**, participants ≥65 YOA not previously vaccinated with ZVL; **N**, number of participants with available results; **M**, month; **IU**, international unit; **Note**: Adapted ATP cohort for Immunogenicity denotes that for each time point presented, the corresponding ATP cohort for immunogenicity was used.

Figure 2. Frequencies of gE-specific CD4[2+] T cells (adapted ATP cohort for immunogenicity) prior to and following RZV vaccination



gE, glycoprotein E; **ATP**, according-to-protocol; **CD4[2+] T cells**, CD4+ T cells expressing at least 2 of the 4 activation markers assessed (interferon-γ, interleukin-2, tumor necrosis factor-α, CD40 ligand); **HZ-PreVac**, participants ≥65 YOA vaccinated with zoster vaccine live (ZVL) ≥5 years earlier; **HZ-NonVac**, participants ≥65 YOA not previously vaccinated with ZVL; **N**, number of participants with available results; **Min/Max**, minimum/maximum; **Q1**, Quartile 1 (25th percentile); **Q3**, Quartile 3 (75th percentile); **M**, month; **Note**: Adapted ATP cohort for Immunogenicity denotes that for each time point presented, the corresponding ATP cohort for immunogenicity was used.

Table 1. Incidence of solicited and unsolicited AEs, SAEs and pIMDs (Total Vaccinated Cohort)

AE (overall/ participant)		Reporting Period	HZ-PreVac		HZ-NonVac	
			N	n (% [95% CI])	N	n (% [95% CI])
Solicited Local AE	Pain	D0–6	215	189 (87.9 [82.8–91.9])	214	181 (84.6 [79.0–89.1])
	Redness		215	96 (44.7 [37.9–51.6])	214	73 (34.1 [27.8–40.9])
	Swelling		215	50 (23.3 [17.8–29.5])	214	37 (17.3 [12.5–23.0])
Solicited General AE	Fatigue		215	114 (53.0 [46.1–59.8])	214	111 (51.9 [45.0–58.7])
	Fever		215	36 (16.7 [12.0–22.4])	214	32 (15.0 [10.5–20.4])
	GI		215	49 (22.8 [17.4–29.0])	214	38 (17.8 [12.9–23.5])
	Headache		215	78 (36.3 [29.8–43.1])	214	89 (41.6 [34.9–48.5])
	Myalgia		215	81 (37.7 [31.2–44.5])	214	77 (36.0 [29.6–42.8])
	Shivering		215	51 (23.7 [18.2–30.0])	214	37 (17.3 [12.5–23.0])
Unsolicited AE	All	D0–29	215	81 (37.7 [31.2–44.5])	215	54 (25.1 [19.5–31.5])
	Related		215	13 (6.0% [3.3–10.1])	215	13 (6.0% [3.3–10.1])
SAE*	All	From D0 to study end	215	18 (8.4 [5.0–12.9])	215	22 (10.2 [6.5–15.1])
pIMD*	All		215	2 (0.9 [0.1–3.3])	215	4 (1.9 [0.5–4.7])

AE, adverse event; **SAE**, serious AE; **pIMD**, potential immune-mediated disease; **HZ-PreVac**, participants ≥65 YOA vaccinated with zoster vaccine live (ZVL) ≥5 years earlier; **HZ-NonVac**, participants ≥65 YOA not previously vaccinated with ZVL; **N**, number of participants with a least one documented (solicited AEs) or administered (unsolicited AEs, SAEs, pIMDs) dose; **n/%**, number/percentage of participants reporting the AE at least once; **95% CI**, exact 95% confidence interval; **GI**, gastrointestinal symptoms (nausea, vomiting, diarrhea and/or abdominal pain); **Fever**, temperature ≥37.5°C for oral, axillary or tympanic route, or ≥38.0°C for rectal route; **D**, day; **D0–6**, 7 days post each dose; **D0–29**, 30 days post each dose; **Related**, AEs assessed by the investigator to be causally related to vaccination; *Up to study end, no SAE and no pIMD were considered causally related to vaccination.

Disclosures. **T. Mrkvan**, GSK: Employee and Shareholder, Salary and shares and share options. **L. Campora**, GSK: Employee and Shareholder, Salary. **G. Catteau**, GSK: Board Member, Salary. **M. Douha**, GSK: Employee, Salary. **K. Grupping**, GSK: Employee, Salary. **C. Herve**, GSK: Employee, Salary. **G. Kalema**, GSK: Consultant, Consulting fee. **T. Heineman**, GSK: Consultant, Employee and Shareholder, Consulting fee and Salary. **N. P. Klein**, GSK: Investigator, Research support. sanofi pasteur: Investigator, Research support. Merck: Investigator, Research support. Pfizer: Investigator, Research support. Protein Science: Investigator, Research support. MedImmune: Investigator, Research support. Dynavax: Investigator, Research support. **H. Lal**, GSK: Shareholder, Salary. Pfizer: Shareholder, Salary. **L. Oostvogels**, GSK: Employee, Salary and stock and stock options. **A. Schuind**, GSK: Employee and Shareholder, Salary.

1957. Pharmacist Prescribing and Care in Patients with Uncomplicated Urinary Tract Infections in the Community: Efficacy and Safety Outcomes of the R_xOUTMAP Study

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Background. Pharmacists have the authorization to prescribe medications for the treatment of uncomplicated urinary tract infections (UTI) in some Canadian provinces. However, there is limited data on the outcomes of this care by pharmacists. Our objective was to evaluate the effectiveness, safety, and patient satisfaction with pharmacist prescribing and care in patients with uncomplicated UTI.

Methods. We conducted a prospective registry trial in 39 community pharmacies in the Canadian province of New Brunswick. Adult patients were enrolled if they presented to the pharmacy with either symptoms of UTI with no current antibacterial treatment (Pharmacist-Initial Arm) or if they presented with a prescription for an antibacterial to treat UTI from another healthcare provider (Physician-Initial Arm). Pharmacists assessed patients and if they had complicating factors or red flags for systemic illness or pyelonephritis, they were excluded from the study. Pharmacists either prescribed antibacterial therapy, modified antibacterial therapy, provided education only, or referred to physician, as appropriate. The primary outcome was clinical cure at 2 weeks and the secondary outcomes included adverse events and patient satisfaction.

Results. A total of 748 patients were enrolled (87% in the Pharmacist-Initial Arm), average age was 40.8 (SD 15.9) years. Clinical cure was achieved in 89% of patients. Of those that did not have sustained symptom resolution, most (6% overall) had symptom recurrence after completion of therapy. Adverse events were reported by 7% of patients and 88% of those continued their medication. Most adverse events were gastrointestinal-related and transient. The patient satisfaction survey reflected very high levels of satisfaction for the care they received, as well as for trust and accessibility of the pharmacist.

Conclusion. Pharmacist management of uncomplicated UTI is effective, safe, and patient satisfaction is very high.

Disclosures. **All authors:** No reported disclosures.

1958. Antiviral Effects, Pharmacokinetics (PK), and Safety of the Respiratory Syncytial Virus (RSV) Fusion Protein Inhibitor, JNJ-53718678 (JNJ-8678), in RSV-infected Infants With Bronchiolitis, in the Phase 1b Study 53718678RSV1005

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Background. JNJ-8678 is a RSV-specific fusion inhibitor and a potential new treatment for respiratory infections caused by RSV. Data from a Phase 1b study of PK, safety and antiviral effects in hospitalized RSV-infected infants are presented.

Methods. 37 and 7 patients, respectively, were randomized to JNJ-8678 (ascending doses, Table) or placebo (PBO) treatment once daily for 7 days. PK assessments were based on sparse sampling using a population PK model in adults scaled for pediatrics, accounting for allometric principles and maturation of drug clearance pathways. Safety was evaluated by AE reporting, lab and ECG assessments. Antiviral activity was assessed by measuring viral load (VL) using a quantitative RT-PCR assay for RSV RNA from nasal swabs.

Results. Sparse PK data are described by an integrated PK model (table) and indicated PK parameters for different dose levels were similar across age groups. Treatment